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(FILE 'HOME' ENTERED AT 11:34:24 ON 12 JUL 2002)

INDEX 'ADISALERTS, ADISINSIGHT, ADISNEWS, AGRICOLA, ANABSTR, AQUASCI,
BIOBUSINESS, BIOCOMMERCE, BIOSIS, BIOTECHABS, BIOTECHDS, BIOTECHNO,
CABA,
CANCERLIT, CAPLUS, CEABA-VTB, CEN, CIN, CONFSCI, CROPB, CROPU, DDFB,
DDFU, DGENE, DRUGB, DRUGLAUNCH, DRUGMONOG2, ...' ENTERED AT 11:34:32 ON
12 JUL 2002

SEA (CARBOXYL-PEG) OR (BIOTIN-PEG) OR (PEG-SILANES) OR
(HETEROF

2 FILE ANABSTR
8 FILE BIOSIS
3 FILE BIOTECHNO
1 FILE CANCERLIT
25 FILE CAPLUS
3 FILE DDFU
4 FILE DGENE
3 FILE DRUGU
3 FILE EMBASE
3 FILE ESBIODBASE
2 FILE IFIPAT
1 FILE JICST-EPLUS
7 FILE MEDLINE
10 FILE SCISEARCH
3 FILE TOXCENTER
44 FILE USPATFULL
6 FILE WPIDS
6 FILE WPINDEX

L1 QUE (CARBOXYL-PEG) OR (BIOTIN-PEG) OR (PEG-SILANES) OR
(HETEROF

FILE 'USPATFULL, CAPLUS, SCISEARCH' ENTERED AT 11:37:35 ON 12 JUL 2002

L2 79 S L1
L3 71 DUP REM L2 (8 DUPLICATES REMOVED)
L4 78078 S L3 AND (FUSION PROTEIN) OR (HYBRID PROTEIN) OR (CHIMER?)
L5 14 S L3 AND (FUSION PROTEIN OR HYBRID PROTEIN OR CHIMER?)

L3 ANSWER 68 OF 71 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1995:196581 CAPLUS

DOCUMENT NUMBER: 122:38832

TITLE: Pharmaceutical liposomes comprising PEG for administration of polypeptides

INVENTOR(S): Zalipsky, Samuel; Martin, Francis

PATENT ASSIGNEE(S): Liposome Technology, Inc., USA

SOURCE: PCT Int. Appl., 53 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------|-----------------|----------|
| WO 9421281 | A1 | 19940929 | WO 1994-US3102 | 19940322 |
| W: AU, CA, JP | | | | |
| RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE | | | | |
| AU 9463683 | A1 | 19941011 | AU 1994-63683 | 19940322 |
| PRIORITY APPLN. INFO.: | | | US 1993-35640 | 19930323 |
| | | | WO 1994-US3102 | 19940322 |
| AB Pharmaceutical liposomes comprising PEG are prepd. for administration of polypeptides. Liposomes contg. biotin-PEG were incubated in the presence of avidin. Avidin-coated liposomes were incubated with biotinylated IgG to obtain liposome-bound antibody. | | | | |

L3 ANSWER 59 OF 71 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1997:164107 CAPLUS

TITLE: Incorporation of PEG-proteins into polymers.

AUTHOR(S): LeJeune, K. E.; Panza, J.; Russell, A. J.

CORPORATE SOURCE: Dept. Chemical Engineering, Carnegie Mellon University, Pittsburgh, PA, 15219, USA

SOURCE: Book of Abstracts, 213th ACS National Meeting, San Francisco, April 13-17 (1997), POLY-182. American Chemical Society: Washington, D.C.
CODEN: 64AOAA

DOCUMENT TYPE: Conference; Meeting Abstract

LANGUAGE: English

AB While the attachment of proteins to polymers is straightforward, their incorporation during polymer synthesis holds several advantages. Unfortunately, the vast majority of polymers occur in harsh org. solvents which have little to no ability to solubilize protein. The attachment of polyethylene glycol to a protein mol. can greatly enhance org. solvent soly. and facilitates protein polymer synthesis. Since a PEG-protein can be dissolved in an org. solvent in close proximity to its native structure

and contains functionalities capable of reacting with a growing polymer chain, the enzyme could become intrinsically coupled to a polymeric material during polymer synthesis. In order to react PEGylated proteins with monomers in org. soln. without significant deleterious effects, a **heterofunctional PEG** must be employed with one end of the PEG designed to couple to a protein and the other with a growing polymer chain. We have synthesized subtilisin polymers through using various **heterofunctional PEG** acrylates. Resultant PEG-subtilisin macromonomers and biopolymers have significant activity retention in both aq. and org. media. Significant enzyme stabilization upon PEG modification and immobilization have also been obsd.

L3 ANSWER 56 OF 71 USPATFULL

ACCESSION NUMBER: 97:89038 USPATFULL

TITLE: Poly(ethylene glycol) and related polymers
monosubstituted with propionic or butanoic acids and
functional derivatives thereof for biotechnical
applications

INVENTOR(S): Harris, J. Milton, Huntsville, AL, United States
Kozlowski, Antoni, Huntsville, AL, United States

PATENT ASSIGNEE(S): Shearwater Polymers, Inc., Huntsville, AL, United
States (U.S. corporation)

| | NUMBER | KIND | DATE |
|-----------------------|--|------|--------------|
| PATENT INFORMATION: | US 5672662 | | 19970930 |
| APPLICATION INFO.: | US 1995-642231 | | 19951002 (8) |
| RELATED APPLN. INFO.: | Continuation-in-part of Ser. No. US 1995-499321, filed on 7 Jul 1995, now abandoned | | |
| DOCUMENT TYPE: | Utility | | |
| FILE SEGMENT: | Granted | | |
| PRIMARY EXAMINER: | Krass, Frederick | | |
| LEGAL REPRESENTATIVE: | Bell, Seltzer, Park & Gibson, P.A. | | |
| NUMBER OF CLAIMS: | 25 | | |
| EXEMPLARY CLAIM: | 1 | | |
| LINE COUNT: | 1103 | | |

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Active esters of PEG acids and related polymers are provided that have
a

single propionic or butanoic acid moiety and no other ester linkages.
These polymer acids have a half life in water of from about 10 to 25
minutes. For example, alpha-methoxy, omega-propionic acid succinimidyl
ester of PEG ("methoxy-PEG-SPA") has a nearly ideal reactivity with
amino groups on proteins and other biologically active substances. The
half life of methoxy-PEG-SPA is about 16.5 minutes in water. The
invention also provides conjugates with proteins, enzymes,
polypeptides,
drugs, dyes, nucleosides, oligonucleotides, lipids, phospholipids,
liposomes, and surfaces of solid materials that are compatible with

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(FILE 'HOME' ENTERED AT 11:04:21 ON 12 JUL 2002)

INDEX 'ADISALERTS, ADISINSIGHT, ADISNEWS, AGRICOLA, ANABSTR, AQUASCI,
CABA, BIOBUSINESS, BIOCOMMERCE, BIOSIS, BIOTECHABS, BIOTECHDS, BIOTECHNO,
CANCERLIT, CAPLUS, CEABA-VTB, CEN, CIN, CONFSCI, CROPB, CROPU, DDFB,
DDFU, DGENE, DRUGB, DRUGLAUNCH, DRUGMONOG2, ...' ENTERED AT 11:04:31 ON
12 JUL 2002

SEA (FUSION PROTEIN) OR (HYBRID PROTEIN) OR (CHIMER?)

1104 FILE ADISALERTS
212 FILE ADISINSIGHT
108 FILE ADISNEWS
3601 FILE AGRICOLA
116 FILE ANABSTR
543 FILE AQUASCI
1264 FILE BIOBUSINESS
591 FILE BIOCOMMERCE
49392 FILE BIOSIS
12935 FILE BIOTECHABS
12935 FILE BIOTECHDS
34353 FILE BIOTECHNO
4830 FILE CABA
23044 FILE CANCERLIT
54414 FILE CAPLUS
1847 FILE CEABA-VTB
53 FILE CEN
667 FILE CIN
914 FILE CONFSCI
10 FILE CROPB
183 FILE CROPU
56 FILE DDFB
2346 FILE DDFU
83326 FILE DGENE
56 FILE DRUGB
438 FILE DRUGNL
3087 FILE DRUGU
275 FILE DRUGUPDATES
521 FILE EMBAL
39825 FILE EMBASE
22984 FILE ESBIODASE
3391 FILE FEDRIP
127 FILE FROSTI
580 FILE FSTA
19443 FILE GENBANK
19 FILE HEALSAFE
4509 FILE IFIPAT
3619 FILE JICST-EPLUS
11 FILE KOSMET
23090 FILE LIFESCI
13 FILE MEDICONF
72637 FILE MEDLINE
27 FILE NIOSHTIC
422 FILE NTIS
74 FILE OCEAN
6153 FILE PASCAL
111 FILE PHAR

5 FILE PHIC
 419 FILE PHIN
 3054 FILE PROMT
 41834 FILE SCISEARCH
 1 FILE SYNTHLINE
 28192 FILE TOXCENTER
 22753 FILE USPATFULL
 118 FILE USPAT2
 7478 FILE WPIDS
 7478 FILE WPINDEX

L1 QUE (FUSION PROTEIN) OR (HYBRID PROTEIN) OR (CHIMER?)

FILE 'BIOSIS, CAPLUS, MEDLINE, EMBASE, SCISEARCH, BIOTECHNO, TOXCENTER,
 LIFESCI' ENTERED AT 11:08:46 ON 12 JUL 2002

L2 633 S L1 AND LINK?(W)REGION
 L3 8 S L2 AND (POLYETHYLENE(W)GLYCOL) OR PEG-NPC OR (X-PEG-Y)
 L4 5 DUP REM L3 (3 DUPLICATES REMOVED)
 L5 83 S L1 AND (LINK?(W)AGENT)
 L6 138958 S L5 AND (PEG) OR (POLYETHYLENE GLYCOL)
 L7 0 S L5 AND PEG
 L8 42 DUP REM L5 (41 DUPLICATES REMOVED)
 L9 0 S L5 AND (POLYETHYLENE(W)GLYCOL)
 L10 16042 S (CROSS(W)LINKING(W)REAGENT)
 L11 67326 S L10 AND (POLYETHYLENE(W)GLYCOL) OR (PEG)
 L12 225 S L10 AND (POLYETHYLENE(W)GLYCOL)
 L13 75 S L10 AND (PEG)
 L14 58 DUP REM L13 (17 DUPLICATES REMOVED)

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L8 ANSWER 39 OF 42 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 13
ACCESSION NUMBER: 1989:587013 CAPLUS
DOCUMENT NUMBER: 111:187013
TITLE: **Chimeric** protein: abrin B chain-trypsin
inhibitor conjugate as a new antitumor agent
AUTHOR(S): Lin, Jung Yaw; Hsieh, Yih Shou; Chu, Shu Chen
CORPORATE SOURCE: Coll. Med., Natl. Taiwan Univ., Taipei, 10018, Taiwan
SOURCE: Biochem. Int. (1989), 19(2), 313-23
CODEN: BIINDF; ISSN: 0158-5231
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Abrin B chain (ANB) and trypsin inhibitor isolated from Acacia confusa
(ACTI) were covalently linked to form a **chimeric** protein
(ANB-ACTI), using N-succinimidyl-3-(-2-pyridyldithio)propionate as
linking agent. The **chimeric** protein had 31%
of the trypsin-inhibitory activity of ACTI and 7% of the hemagglutinating
activity of ANB but caused no inhibition of protein biosynthesis.
ANB-ACTI had strong inhibitory effects on the growth of sarcoma 180 cells
and Hela cells in culture, while the mixt. of an equiv. amt. of free ANB
and ACTI did not. Thus, the ANB of the **chimeric** protein may act
as a vector to carry ACTI into the tumor cells. The incorporation of
ACTI
into the **chimeric** protein potentiates its antitumor activity as